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RECENT SOVIET WORK ON TULAREMIA

[Comment: In the January 1954 issue of the Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii, the editors announced the subjects to be discussed in each of the 1954 issues of the journal. The main subject of issue No 2 was to be tularemia. The following report is a summary of the five articles on tularemia which appeared in issue No 2 and of five other articles on tularemia published in issues No 3 and 4.]

Numbers in parentheses refer to appended sources.]

A. S. Shevelev of the Chair of Microbiology of the Smolensk Medical Institute and the Smolensk Institute of Epidemiology and Microbiology investigated the effects of drug-induced sleep and narcotic inhibition on allergy reactions and on the production of antibodies during the interval between inoculation and the establishment of active immunity.

A series of three experiments was conducted, using 50 guinea pigs. All of the animals were first inoculated with a tularemia vaccine. Then, 18 of them were used as a control group, while the other 32 were administered a 5% aqueous solution of medinal [barbital sodium] at the rate of 0.015 gram per 100 grams of body weight for various lengths of time.

In the first experiment, the animals were kept in a state of sleep for 16-18 hours, awakened, kept conscious for 6-7 hours, and then put to sleep again for an additional 13-18 hours. No significant changes in the immunological reactions of the animals were observed. This, according to the author, illustrated the relatively slight effect of normal sleep on these reactions. In the second experiment, the animals were kept asleep intermittently over a period of 3 days. They were awakened and kept conscious for 6-7 hours each day. In the third experiment, the animals were kept asleep uninterruptedly for 30 hours. The animals did not lose their sensitivity to pain, i.e., did not undergo complete narcosis, in any of tne experiments, although several of them died from intoxication during the second experiment.

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Tests conducted on the sleeping animals showed that the drug-induced sleep inhibited the development of allergic reactions and suppressed the normal production of antibodies. The author concludes that the suppression of immunological reactions was due to an inhibiting action of the drug on the central nervous system and not to subsequent intoxication. In the second experiment, in which the animals received an extremely large amount of the drug, the immunological reactions were suppressed less than they were in the third experiment.(1)

V. A. Yudenich of the Chair of Microbiology of the Smolensk Medical Institute submitted a report on revaccination against tularemia. He stated that Gayskiy, El'bert, Faybich, Zlatkovskiy, Olsuf'yev, and Mayskiy reported that persons vaccinated with a living tularemia vaccine were found to be immune for at least 4-5 years. On the basis of these reports, at a conference called in Moscow 11 and 12 June 1951 by the Ministry of Health RSFSR to discuss the effectiveness of inoculations against tularemia, a resolution was passed to the effect that groups of persons vaccinated against tularemia should not be revaccinated for at least 4 years, and then only if immunological reaction tests showed that more than 25% of the group no longer reacted positively to tulyarin (Soviet-produced tularin).

Sufficient time having elapsed since the completion of the first large-scale vaccinations, Yudenich made a detailed study of the duration of immunity and of the phenomena connected with it. He found that persons vaccinated with the living tularemia vaccine exhibited a positive allergic reaction to subcutaneous injections of tulyarin, or small amounts of the vaccine, for from 4 to 5 years. Revaccination of such persons produced violent allergic reactions, which, in some instances, incapacitated the person for several days. Cutaneous vaccination of persons who had recovered from tularemia earlier produced severe allergic reactions and, in most cases, general reactions such as the enlargment of local lymph glands.(2)

Another report on the duration of immunity and revaccination was given by R. Ya. Bondar' of the Odessa Institute of Vaccines and Serums. He found that 83.2% of persons, 14 years old or older, who had been vaccinated by Elbert's procedure with Gayskiy's egg-yolk tularemia vaccine, exhibited a positive reaction to an intracutaneous injection of tulyarin for as long as 2 years, and 58% of them showed positive agglutination reactions. After the same period of time, only 34.3% of the children between the ages of 7 and 14 reacted positively to the tulyarin test. In the author's opinion, these reactions are an indication of immunity, and persons reacting negatively to the tulyarin skin test should be revaccinated against tularemia.(3)

N. G. Olsuf'yev and O. S. Yemel'yanova of the Tularemia Laboratory of the Division of Parasitology and Medical Zoology of the Institute of Microbiology and Epidemiology imeni Gamaleya reported on mixed epizootics of tularemia among common field mice during winter 1951-1952. Bacteriological examinations of dead mice found in hay stacks and straw revealed that they had been infected not only with tularemia, but with listerellosis and streptococcosis as well. In the area where the mice were found to be infected with listerellosis, a sheep contracted listerellosis at the same time. Cultures of listeria isolated from both the mice and the sheep were completely identical.

The authors commented that the presence of mixed epizootics among rodents should be studied by epidemiologists and specialists in infectious diseases since mixed infections in humans, i.e. infection with both tularemia and listerellosis, might be connected with such epizootics.

M. M. Gerasimova of an unspecified oblast' antitularemia station reported an outbreak of tularemia which occurred at threshing time and was apparently caused by contaminated rye.

The outbreak occured in one of rayons of the northern forest belt during the middle of September, while the rye was being threshed, and lasted about 6 days. The clinical course of the disease indicated that the persons afflicted were suffering from tularemia. The internal organs and the respiratory tract were affected. Agglutination reactions with standard tularemia diagnostic preparations were positive in all cases in titers of 1:800-1:1600. The rye did not become contaminated while in stacks, rather during the short time that the sheaves lay in the field. This assumption is based on the fact that the rye was threshed immediately after it was cut.(5)

Another report on winter epizootics of tularemia is given by L. A. Pomanskaya also of an unidentified oblast' antitularemia station. She describes an epizootic of tularemia among mouselike rodents during winter 1952-1953.

Cultures were made directly from the organs of animal corpses delivered in a frozen state to the laboratory, and the etiological agent causing the epizootic was rapidly diagnosed as Pasteurella tularensis.

Cultures of P. tularensis were isolated without any difficulty from 69 grey polevki [Microtus arvalis], 3 dwarf mice [Micromys minutus], 2 field mice [Apodemus agrarius], and one house mouse [Mus musculus]. An additional culture was obtained from Gamasidae taken from the dead animals. All the strains isolated were typical and possessed a high virulence. A dose equivalent to one bacterial cell infected subcutaneously killed white mice within 5-6 days. A dose equivalent to ten bacterial cells was sufficient to kill guinea pigs.(6)

V. B. Plakhova of the Tomsk Scientific Research Institute of Vaccines and Serums discussed various procedures for bringing about specific precipitation reactions to be used in diagnosis tularemia.

A ring precipitation reaction (similar to Ascoli's reaction) to be used for the diagnosis of tularemia in water rats was first proposed by Zarkhi in 1928. This reaction later found wide application. Khatenever, Tolstukhina, and others used it to detect the etiological agent of tularemia among wild rodents. Yemel'yanova used it to identify cultures which had been isolated from suspected animals.

In 1945, Karpov and Konnikov proposed a modified reaction which utilizes a hapten. This reaction turned out to be much more sensitive than Zarkhi's reaction.

According to Zarkhi's method, a thermoextract, obtained by heating a suspension of the lymph glands and spleens of infected animals on a water bath at 100°C for 5-8 minutes, is filtered and poured in a layer above an equal quantity of precipitating or agglutinating serum. According to Karpov and Konnikov's method, 4 drops of cresol red, an indicator, are added to the suspension after it has been heated on the water bath. Next, a 10% solution of hydrochloric acid is added, until the liquid assumes a rosy tint. The acidified suspension is than placed on the water bath for an additional 12 minutes. After this, it is neutralized by adding a 4% solution of NaOH, until it assumes a violet tint. The processed extract is filtered through paper and used to produce a precipitation reaction with antitularemia serum.

Extensive laboratory experiments have shown that the precipitation reaction employing hapten is much more specific and rapid than Zarkhi's reaction. The author therefore recommended it as a sensitive method of diagnosing tularemia.(7)

During winter 1949, G. A. Zeygermakher of an unspecified rayon sanitary epidemiological station observed an outbreak of tularemia in one of the southwest rayons of the Ukraine. The outbreak occured among adult members of the

rural population. Of those who became ill, 98% contracted the visceral form of the disease. Since the outbreak was not connected with the threshing of grain, the authors were of the opinion that the disease was caused by micro-organisms present on straw, corn stalks, and sunflower stalks used for fuel.(8)

N. N. Lang and A. P. Semenova of the Rostov Oblast' Antitularemia Station discussed the modifications of the tularemia bacteria which occur during inter-epidemic periods. They showed that a decrease in the rodent population, due to epizootics and other causes, was accompanied by a decrease in the percentage of animals infected by P. tularensis and an increase in the number of atypical strains of P. tularensis. The latter no longer agglutinate specific tularemia serums and produce antigens similar to those produced by the group of micro-organism causing hemorrhagic septicemia. The atypical strains also grow better on agar and exhibit a greater fermentative activity than ordinary strains.(9)

Ye. A. Dem'yanov and M. M. Dem'yanova of the Mikhaylovskaya Antitularemia Station reported that they had devised a rapid method for diagnosing tularemia in animals. They used an antigen prepared from the organs of rodents to cause an agglutination reaction. The antigen is prepared by taking one gram of spleen (plus pieces of the liver, if the spleen is not large enough), carefully grinding it in a mortar with 9 ml of physiological salt solution, placing the resultant emulsion on a boiling water bath for 2-30 minutes, and filtering it through a paper filter. The antigen can also be prepared from the mummified corpses of rodents.

Tularemia serum agglutinates this antigen after 3-5 hours at a temperature of 37°C. The reaction, according to the authors, is specific, and can be used to confirm the existence of tularemia epizootics among rodents. In tests on 132 naturally infected animals from epizootic locales and on experimental animals, the agglutination reaction yielded 100% positive results; a precipitation reaction yielded only 91%; microscopic examinations, 76%; and attempts at culturing, 12%. (Warning is given that this proposed for the rapid diagnosis of tularemia among rodents is still in need of further testing and has not yet been recommended for introduction into actual practice. -- The editors of Zhurnal Mikrobiologii, Epidemiologii, i Immunobiologii.) (10)

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